REMARKS

Reconsideration and reexamination of this application are respectfully requested.

The listing of claims cancels claims 1-14, without prejudice or disclaimer, and amends claims 15, 20, 24, and 25. Applicants reserve the right to prosecute claims 1-14 or similar claims in a continuation or divisional application. The amendments to claims 15, 20, 24, and 25 find support in the specification as filed, such as in the claims as filed, and do not introduce new matter. Claims 15-26 are pending.

A. The Rejections Under 35 U.S.C. § 112, Second Paragraph, Should Be Withdrawn.

Claims 24-26 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite on the basis of their recitation of "stimulus," which the Examiner alleged lacks an antecedent basis in the claims from which claims 24-26 depend. (Office Action at Paragraphs 15-18.) Applicants have amended the claims to recite "treatment" rather than "stimulus" thus obviating the basis for the rejection. Applicants request that this rejection be withdrawn.

Claims 24-26 were also rejected as allegedly indefinite because the Examiner contends that "'side effect distance' and 'on-target distance'" are "vague and indefinite." According to the Examiner, "[i]t is unclear what these distances are measured in relation to."

Applicants note that claim 26 depends from claim 25, which depends from claim 24, which depends from claim 23, which depends from claim 22. Claim 22 recites

"determining a side effect distance in a multivariate space between the side effect signature and the control side effect signature." Claim 23 recites "determining a target effect distance in a multivariate space between the on-target effect signature and the control on-target effect signature." Applicants agree with the Examiner's implicit determination that those recitations in claims 22 and 23 are definite. Applicants submit that it is clear that claims 24-26 refer back to those recitations when claims 24-26 recite "side effect distance" and "on-target distance." Thus, Applicants submit that claims 24-26 are definite and request that this basis of rejection be withdrawn.

B. <u>The Rejection Under 35 U.S.C. § 101 Should Be Withdrawn.</u>

Claims 15-26 were rejected under 35 U.S.C. § 101 as allegedly directed to non-statutory subject matter. (Office Action at Paragraphs 19-26.) Specifically, the Examiner stated that, "Claims 15-26 are drawn to methods which characterize a treatment applied to cells via imaging the cells, identifying signatures as a result of the treatment or lack thereof, and calculating metrics. These claims produce a result which does not meet the standard of being concrete, tangible and useful, as required." Applicants respectfully traverse the rejection.

As amended, claim 15 recites applying a treatment to a population of cells and deriving a plurality of cellular features from at least a first captured image of the population of cells that have been exposed to the treatment. The claim further recites "creating an on-target effect signature" and "creating a side effect signature." The claim further recites "creating an on-target effect metric derived from the on-target effect

signature" and "creating a side effect metric derived from the side effect signature." Finally, the claim recites "comparing the on-target effect metric to the side effect metric to thereby characterise the treatment." Applicants submit that by "comparing . . . to thereby characterise the treatment" the claimed method is concrete, tangible and useful. As stated at paragraph 0007 of the specification, the invention, among other things, provides a method that allows investigating, characterising or classifying the effects and side effects of treatments on cells.

Applicants note that the Examiner included a lengthy discussion of standards applied to inventions that may be performed by a computer. Applicants submit that the claimed methods certainly may be performed using a computing device. The claimed methods may also be performed in other ways, including in other ways that do not utilize a computing device.

Applicants submit that the claimed methods satisfy the utility requirement and respectfully request that the rejection be withdrawn.

C. <u>The Rejection Under 35 U.S.C. § 103 Should Be Withdrawn.</u>

Claims 15-23 were rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Johnson (US Patent No. 6611833) in view of Friend et al. (US Patent No. 6,801,856). (Office Action at Paragraphs 3-14.) After stating many characterizations of the disclosures of Johnson and Friend, the Examiner supported this rejection stating:

> It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have implemented the invention of Johnson where images of

> "normal" and "abnormal" cell tissues are taken and the quantitative properties of cellular features are measured to form indices that can be accessed and used for comparison. One of skill in the art would have been motivated to use such a system of categorizing cellular data since image analysis can reveal data about cellular states. One of skill in the art would have had the further motivation to treat the cells with various doses of drug candidates and determine the responses with image analysis as taught by Friend. The classification of image data as taught by Johnson is not limited to tissue that is "normal" or "abnormal" and can be used to categorize and study the cellular expected or unexpected side effect response of cells when subjected to drug treatment. One of skill in the art would have had a reasonable expectation of success at using the imaging and measurement of quantitative characteristics of cells as taught by Johnson on the drug candidate treated cells of Friend et al. The multivariate space calculations as taught by friend el al. could have also formed the indices of quantitative values forming the database in Johnson et al. Therefore, the invention as a whole would have been prima facie obvious, absent evidence to the contrary.

(Office Action at Paragraph 14.)

Applicants respectfully traverse the rejection. During Examination "The examiner bears the initial burden of factually supporting any *prima facie* conclusion of obviousness. If the examiner does not produce a *prima facie* case, the applicant is under no obligation to submit evidence of nonobviousness." M.P.E.P. § 2142. "To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined)

must teach or suggest all the claim limitations." M.P.E.P. § 2142. Applicants will show that the Officer has not met *any* of the required elements to make out a case of *prime facie* obviousness.

Amended claim 15, and claims 16-26 as they depend from claim 15, recite "creating an on-target effect signature, which is characteristic of an on-target effect of the treatment on the population of cells, from at least a first one of the plurality of cellular features" **and** "creating a side effect signature, which is characteristic of a side effect to the on-target effect, from at least a second one of the plurality of cellular features." The recitation "cellular feature" in those passages is defined earlier in the claim, by the recitation "deriving a plurality of cellular features from at least a first captured image of the population of cells that have been exposed to the treatment." Thus, the on-target effect signature and the side effect signature are both derived from the same population of cells. The claims also recite "comparing the on-target effect metric to the side effect metric to thereby characterise the treatment."

As described at paragraph 0030 of the specification, an on-target effect is an expected or intended effect under investigation for a treatment on cells. In contrast, as described at paragraphs 0039 and 0040, a side effect is an effect on a cellular feature that is not related to an intended or on-target effect under investigation.

In contrast to the claims, Johnson does not derive both an on-target effect signature and a side effect signature from the same population of cells following a treatment. Instead, Johnson is analyzing "normal" and "abnormal" tissues—which are

different cell populations. The Examiner acknowledges this distinction between Johnson and the claimed invention at Paragraph 7.

The Examiner relies on Friend primarily for the alleged teaching of "building 'consensus profiles' for response of cells to various drugs by exposing them to graded levels of the drugs (col. 6, lines 1-19)." As quoted above, the Examiner then leaps to the conclusion that "The classification of image data as taught by Johnson is not limited to tissue that is 'normal' or 'abnormal' and can be used to categorize and study the cellular expected or unexpected side effect response of cells when subjected to drug treatment." (Office Action at Paragraph 14.) Missing from that conclusion is any explanation of what would have motivated the skilled artisan to make such a modification of the teachings of Johnson and Friend.

In that regard, Applicants respectfully remind the Examiner that Applicants' own teachings can not be relied on as a motivation to modify and combine teachings in the prior art to arrive at Applicants' invention. *See* M.P.E.P. § 2143. Here, the Examiner seems to imply that just because the skilled artisan could have, in the Examiner's view, modified the teachings of the art, to do so would have been obvious. However, the mere ability to make the modification is not sufficient to make out a *prime facie* case. *See* 2143.01 (IV).

Applicants submit that numerous prior art methods, including methods known decades if not centuries before their invention, relied upon a comparison of normal and abnormal tissues in some way, just as the methods of Johnson. In contrast to those old methods, Applicants' claimed methods include treatment of a population of cells and

"creating an on-target effect signature, which is characteristic of an on-target effect of the treatment on the population of cells, from at least a first one of the plurality of cellular features" and "creating a side effect signature, which is characteristic of a side effect to the on-target effect, from at least a second one of the plurality of cellular features." The claimed methods then recite "creating an on-target effect metric derived from the on-target effect signature; creating a side effect metric derived from the side effect signature; and comparing the on-target effect metric to the side effect metric to thereby characterise the treatment." Neither Johnson nor Friend, alone or in combination, disclose or suggest a method combining those aspects to characterize a treatment applied to a population of cells. And nothing in the references suggests modifying the teachings of the references to arrive at a method which combines the elements as claimed. Accordingly, the Office has not made out a case of *prime facie* obviousness and the rejection for alleged obviousness should be withdrawn.

D. Conclusion.

In view of the foregoing amendments and remarks, Applicants respectfully requests reconsideration and reexamination of this application and the timely allowance of the pending claims 15-26.

Please grant any extensions of time required to enter this response and charge any additional required fees to Deposit Account No. 06-0916.

Respectfully submitted,

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